WS14.5 Influence of breathing pattern on pulmonary aerosol deposition in patients with cystic fibrosis (CF): a pharmacokinetic approach

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The therapeutic effect of inhaled antibiotics on lung infection in CF patients is dependent on the aerosol deposition achieved in the lungs.

Objectives: To evaluate the influence of two breathing patterns on pulmonary aerosol deposition using pharmacokinetic parameters as surrogate for deposition.

Methods: In a randomized, open-label, crossover study pulmonary deposition in 18 adult CF patients is evaluated following inhalation of tobramycin aerosol using the I-neb nebulizer with TBM (Tidal Breathing Mode) and TIM (Target Inhalation Mode) breathing patterns. Breathing in TIM forced the patient to inhale in a slow and deep manner. According to their lung function, patients were categorized in subgroup 1, 2 or 3 corresponding to FEV1 predicted $\leqslant$59%, 60–79% or $\geqslant$80%. Blood samples were collected in order to model tobramycin pharmacokinetics.

Results: Mean C_{max} and AUC_{0-24hr} were significantly increased for TIM compared to TBM. Inhalation in TIM also resulted in higher mean C_{max} and AUC_{0-24hr} for each subgroup. Mean bioavailability of TIM relative to TBM breathing pattern (F_{rel}) was 1.53$\pm$0.41 and mean F_{rel} in each subgroup was also significantly higher than 1. Subgroup category did not affect the results.

Conclusion: Slow and deep inhalation of aerosolized tobramycin with the I-neb nebulizer resulted in an estimated 53% higher lung deposition compared to tidal breathing. This result was independent from lung function category, which suggests that regardless the disease state, slow and deep inhalation always results in higher pulmonary aerosol deposition compared to tidal breathing.

WS14.6 Feasibility study to objectively measure airway clearance technique in cystic fibrosis

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Background: Suboptimal airway clearance technique (ACT) in CF (poor adherence and/or poor technique) can limit its effectiveness, yet airway clearance has always been "invisible". The Acapella® is a common ACT device.

Objectives:

1. Test the feasibility of using an electronic data capture (EDC) system to objectively measure the use of Acapella® and comparing it against self-report.
2. Use EDC to explore adherence and technique (blow duration and flow rate).

Methods: Unblinded before and after exploratory study using an EDC system among 10 adults with CF. The EDC system consists of a pressure transducer that records air-flow, date and time. It is inserted between the mouthpiece and body of the Acapella®. It has a beeper that can be programmed to provide feedback with an audible beep with every satisfactory blow i.e. breath exhalation with flow rate $\geqslant$20 L/min that reached the target duration of 3 s.

In the 1st phase, all participants used the EDC without any feedback. In the 2nd phase, the beeper was turned on to provide immediate feedback when the Acapella® was used. In both phases, participants reported their estimated daily Acapella® use with a questionnaire. Data collection is ongoing.

Results: Objective EDC suggested that self-report over-estimated adherence. Patients found it difficult to achieve adequate blows but beeper feedback improved technique. The table presents illustrative data.

Table: Illustrative results from 1 participant

	Participant 1	
	Phase 1	Phase 2
Follow-up duration, days	4	11
Agreed number of daily blows	20	20
Self-report number of daily blows (% adherence)	20 (100)	20 (100)
Objective (EDC) average number of daily blows (% adherence)	9 (45)	3 (15)
Objective (EDC) total number of blows	36	34
Objective (EDC) total number of satisfactory blows	24	34
Percentage of satisfactory blows (%)	67%	100%

Conclusion: Objective measure of ACT is possible. Feedback may improve the quality of ACT.

Acapella® is a registered trademark of Smiths Medical ASD Inc which supported this study.